Incremental Value of the Preoperative Echocardiogram to Predict Mortality and Major Morbidity in Coronary Artery Bypass Surgery

Running title: Afilalo et al.; Echocardiography Before Coronary Bypass Surgery

Jonathan Afifalo, MD, MSc1,2; Aidan W. Flynn, MD, PhD1; Avi Shimony, MD2; Lawrence G. Rudski, MD2; Arvind K. Agnihotri, MD3; Jean-Francois Morin, MD4; Cristina Castrillo, MD1; David M. Shahian, MD3,5; Michael H. Picard, MD1

1Cardiac Ultrasound Laboratory, Div of Cardiology; 2Div of Cardiac Surgery; 3Div of Cardiac Surgery, Jewish General Hospital, McGill University, Montreal, Canada

Address for Correspondence:
Jonathan Afifalo, MD, MSc
Massachusetts General Hospital
55 Fruit Street, Yawkey 5E
Boston, MA  02114
Tel: (617) 726-2000
Fax: (617) 249-1774
E-mail: jonathan@afilalo.com

Journal Subject Codes: [7] Chronic ischemic heart disease; [31] Echocardiography; [36] CV surgery: coronary artery disease; [100] Health policy and outcome research
Abstract:

Background—Although echocardiography is commonly performed before coronary artery bypass surgery (CABG), there has yet to be a study examining the incremental prognostic value of a complete echocardiogram.

Methods and Results—Patients undergoing isolated CABG at two hospitals were divided into derivation and validation cohorts. A panel of quantitative echocardiographic parameters was measured. Clinical variables were extracted from the STS database. The primary outcome was in-hospital mortality or major morbidity, and the secondary outcome was long-term all-cause mortality. The derivation cohort consisted of 667 patients with a mean age of 67.2±11.1 years and 22.8% females. The following echocardiographic parameters were found to be optimal predictors of mortality or major morbidity: severe diastolic dysfunction as evidenced by restrictive filling (OR 2.96; 95% CI 1.59,5.49), RV dysfunction as evidenced by fractional area change <35% (OR 3.03; 95% CI 1.28,7.20) or myocardial performance index >0.40 (OR 1.89; 95% CI 1.13,3.15). These results were confirmed in the validation cohort of 187 patients. When added to the STS risk score, the echocardiographic parameters resulted in a net improvement in model discrimination and reclassification with a change in c-statistic from 0.68 to 0.73 and an integrated discrimination improvement of 5.9% (95% CI 2.8%, 8.9%). In the Cox proportional hazards model, RV dysfunction and pulmonary hypertension were independently predictive of mortality over 3.2 years of follow-up.

Conclusions—Preoperative echocardiography, in particular RV dysfunction and restrictive LV filling, provides incremental prognostic value in identifying patients at higher risk of mortality or major morbidity after CABG.

Key words: echocardiography; outcomes research; revascularization; right ventricular function; surgery
Introduction

One in 7 patients suffers a major complication or death after coronary artery bypass graft surgery (CABG), and available cardiac surgery risk scores are often not able to identify these patients in advance. Identification of high-risk patients and subsequent tailoring of the revascularization strategy and post-operative management may be aided by an assessment of cardiac structure and function such as by echocardiography. However, risk scores encompass very few echocardiographic parameters; the Society of Thoracic Surgeons (STS) risk score includes left ventricular ejection fraction (LVEF) and significant valvular regurgitation or stenosis, whereas the EuroSCORE includes LVEF and pulmonary arterial hypertension.

Professional society guidelines have limited comments on the practice of routine preoperative echocardiography; as a result, there is significant variability among practitioners and institutions. The 2011 ACC/AHA CABG Guidelines do not provide specific recommendations for preoperative echocardiography whereas the preceding 2004 Guidelines listed it as a level IIb recommendation (usefulness less well established) in a limited subset of patients with recent anterior myocardial infarction. Furthermore, the 2011 ACC/AHA/ASE Appropriateness Criteria provide recommendations for echocardiography before noncardiac surgery but do not address echocardiography before CABG.

No previous studies thoroughly evaluated the prognostic information that can be gained from a comprehensive preoperative echocardiogram. Such a study would demonstrate the independent value of each parameter, and the incremental value of the echocardiogram as a whole when added to traditional risk scores. With this new information, guideline committees would have a stronger evidence base upon which to justify more definitive recommendations. Given this context, the objective of this study was to identify echocardiographic predictors of
mortality and major morbidity in patients undergoing isolated CABG, and to determine the incremental prognostic value of the echocardiogram in addition to traditional risk scores.

Methods

Study design
A cohort of patients undergoing isolated CABG at two university hospitals in the United States and Canada between 2007 and 2011 was assembled. Preoperative echocardiograms were reviewed to test the hypothesis that echocardiographic parameters would add incremental value above traditional cardiac surgery risk scores to predict postoperative mortality or major morbidity. A comprehensive echocardiographic panel was measured in the derivation cohort to identify optimal parameters, and subsequently verified in the validation cohort.

Setting
The derivation cohort consisted of consecutive patients who underwent isolated CABG at the Massachusetts General Hospital between January 1 2007 and December 31 2009. The validation cohort consisted of consecutive patients who underwent isolated CABG at the Jewish General Hospital between September 1 2010 and July 11 2011. Patients in both cohorts were followed from the time of their index admission to hospital discharge; additionally, patients in the derivation cohort were followed forward for vital status up to July 1 2011.

Participants
The inclusion criteria were: (1) isolated CABG defined as coronary artery bypass surgery without concomitant repair or replacement of the heart valves or great vessels, and (2) preoperative transthoracic echocardiogram performed at the study center ≤30 days before surgery. Since echocardiographic images were re-analyzed for the purpose of this study, patients
were excluded if they only had echocardiographic reports from an outside center or if their
digital echocardiographic images could not be retrieved for technical reasons.

**Predictor variables**

A comprehensive list of quantitative parameters of left- and right-sided chamber size, geometry,
systolic and diastolic function, and valvular function were measured from the preoperative
echocardiogram. The echocardiographic protocol and normal reference limits adhered to the
guidelines of the American Society of Echocardiography6-10. Right and left atrial areas were
measured at end-systole in the apical 4-chamber view; left atrial height was also measured to
calculate left atrial volume using the single-plane area-length method. Right ventricular (RV)
area was measured at end-diastole and end-systole in the apical 4-chamber view and fractional
area change (FAC) was calculated as: \[ RV \text{ end-diastolic area} - RV \text{ end-systolic area} / [RV \text{ end-}
\text{diastolic area}] \). Tricuspid valve closure to opening time was measured by continuous wave
Doppler of the tricuspid regurgitation and/or pulsed Doppler of the tricuspid inflow. Pulmonic
ejection time was measured by pulsed Doppler of the distal RV outflow tract. RV myocardial
performance index (MPI), an index of RV efficiency reflecting both systolic and diastolic
function, was calculated as: \[ \text{Tricuspid valve closure opening time} - \text{Pulmonic ejection time} / \text{Pulmonic ejection time} \]. Pulmonary artery systolic pressure (PASP) was measured by
continuous wave Doppler of the tricuspid regurgitation with 10 mmHg added for right atrial
pressure. LVEF was measured using the biplane Simpson’s method. LV mass was measured
using the Devereux method. LV diastolic function was assessed using a multi-parametric
approach including pulsed Doppler of the mitral and pulmonary vein inflow, tissue Doppler of
the medial and lateral annulus, and left atrial volume. Valvular regurgitation and stenosis were
assessed using a multi-parametric approach as reported by the echocardiography reader including
mean and peak gradients, color Doppler jet appearance, vena contracta, and proximal isovelocity shell area (PISA) where applicable.

Measurements were performed in duplicate by two independent echocardiography readers (JA, AF, CC, AS), and arbitrated by a third senior reader (MHP, LGR). All readers were cardiologists trained in echocardiography. To ensure accuracy and consistency of measurement techniques, readers participated in focused training sessions and quality audits throughout the study. Readers were blinded to the clinical data and outcomes when interpreting the echocardiograms.

Outcome variables

The primary outcome was a composite of in-hospital mortality or major morbidity defined according to the STS data definitions as any one of the following: all-cause death, stroke, renal failure, prolonged ventilation, deep sternal wound infection, or need for reoperation. The secondary outcome was long-term all-cause mortality defined as death from any cause occurring from the time of cardiac surgery to the end of follow-up. There were no patients lost to follow-up for the primary or secondary outcomes.

Data sources

Echocardiographic measurements were performed on the digital echocardiographic images stored on dedicated servers. Echocardiograms were performed with the Philips IE33, Sonos 7500, or GE Vivid 7 machines and analyzed on the Xcelera workstation (Philips Medical Systems, Andover, MA) at the derivation site, and with the GE Vivid 7 machine and EchoPAC workstation (GE, Milwaukee, WI) at the validation site. Clinical data, including in-hospital outcomes, were extracted according to the STS Adult Cardiac Surgery Database. Vital status was extracted from the Social Security Death Index by way of the Research Patient Data
Registry (Partners Healthcare, Boston, MA).

**Study size**

Assuming a baseline incidence of mortality or major morbidity of 14.4%\(^1\), 430 patients were needed to demonstrate an odds ratio of at least 1.5 with a two-sided alpha of 0.05 and a beta of 0.2 in our multivariable regression model. Moreover, since the multivariable model was prespecified to contain up to 11 covariables (10 echocardiographic parameters plus the STS-Predicted Risk of Mortality or Major Morbidity (STS-PROMM)), approximately 110 events were required to maintain an appropriate covariable:event ratio to avoid overfitting\(^12\).

**Statistical methods**

Echocardiography variables were preserved in their continuous form\(^13\) and standardized such that the resulting odds ratios represented the increase in odds per standard deviation in that variable. To test the appropriateness of entering a continuous variable in a logistic regression model, each echocardiographic variable (x-axis) was plotted against the logit of the primary outcome (y-axis) and the resulting graphical plot was inspected for linearity. Since clinicians often utilize cutoffs in day-to-day practice, echocardiography variables were also dichotomized according to accepted normal reference limits and analyses were presented using both continuous and dichotomized predictors.

The multivariable echocardiographic model was *a priori* prespecified to include one parameter from each of the following domains: right atrial size, RV size, RV systolic function, RV diastolic function or MPI, PASP, tricuspid regurgitation, left atrial size, LV size, LV systolic function, LV diastolic function, LV mass, and mitral regurgitation. Indexed parameters were used and volumes/areas were favored over linear dimensions for cavity size. Right and left atrial size were removed from the model as they were found to be intermediate factors in the causal
pathway between diastolic dysfunction and adverse outcomes, and also between tricuspid/mitral regurgitation and adverse outcomes (leading to model instability and over-adjustment bias when entered\textsuperscript{14}).

For the primary outcome, a multivariable logistic regression model was used to identify the optimal echocardiographic parameters to predict in-hospital mortality or major morbidity. For the secondary outcome, a multivariable Cox proportional hazards model was used to identify the optimal echocardiographic parameters to predict all-cause mortality. The proportionality of hazards assumptions was tested based on Schoenfeld residuals. Of note, these echocardiographic models did not contain clinical variables or the STS-PROMM.

To test the incremental predictive value for mortality or major morbidity, the optimal echocardiographic parameters identified in the above model were then entered in a subsequent model that contained the STS-PROMM. Model performance statistics were calculated before and after addition of the echocardiographic parameters to STS-PROMM. These statistics included the c-statistic for discrimination, Aikaiikes Information Criterion (AIC) for global fit, Net Reclassification Improvement (NRI) and Integrated Discrimination Improvement (IDI) for reclassification\textsuperscript{15}. For the NRI, the Q1 and Q3 were used to define STS-PROMM cutoffs: low risk 0-10\%, intermediate risk 10\%-25\%, and high risk >25\%. The AIC approach with forward selection was used to select the echocardiographic variables for the model, with the optimal model being that which minimized the AIC.

The model selected and coefficients identified in the derivation cohort were applied to predict the risk of mortality or major morbidity in the external validation cohort. The c-statistic for these predicted probabilities in the validation cohort was calculated and compared to the c-statistic for the STS-PROMM alone.
Sensitivity analysis was performed in which the echocardiographic parameters were entered in a model containing individual clinical covariables rather than the composite STS-PROMM. The clinical covariables were chosen to be those with the highest coefficients in the STS-PROMM model (age, female, diabetes, chronic kidney disease, chronic lung disease, peripheral arterial disease, cerebrovascular disease, atrial fibrillation, prior cardiac surgery). Measurements were >90-95% complete for all echocardiographic parameters, with the exception of PASP (74% complete, not measurable when no tricuspid regurgitation). Therefore, a sensitivity analysis was performed in which multiple imputation was used to derive missing values for PASP. All analyses were performed with STATA 12 (College Station, TX).

Results

Derivation Cohort

A total of 1,150 patients underwent isolated CABG at the derivation site between 2007-2009, of which 667 had available echocardiograms performed at the study center ≤30 days before surgery (mean 5.6 ± 5.8 days before surgery) (Figure 1). Those who did not have available echocardiograms at the study center were excluded; they had determination of left ventricular function by angiocardiography (N=387), echocardiography at another center (N=49), nuclear medicine (N=33), or other modality (N=14), and were less likely to present with myocardial infarction, have heart failure, or require urgent surgery (Supplementary Table 1).

Baseline clinical characteristics are shown in Table 1. The mean age was 67.2 ± 11.1 years with 10.0% octogenarians and 22.8% females. Patients were evenly distributed in low risk (29% with STS-PROMM 0-9%), intermediate risk (46% with STS-PROMM 10-25%), and high risk (25% with STS-PROMM ≥25%) categories. One-hundred-and-four (15.6%) postoperative
mortalities or major morbidities were observed during the index hospitalization.

The preoperative echocardiographic parameters are shown in Table 2. The optimal echocardiographic model to predict in-hospital mortality or major morbidity consisted of: restrictive LV diastolic filling (OR 2.39; 95% CI 1.26, 4.55), RV fractional area change (OR 0.73; 95% CI 0.56, 0.95), RV myocardial performance index (OR 1.44; 95% CI 1.10, 1.90), and mitral regurgitation (OR 1.44; 95% CI 1.04, 2.01) although mitral regurgitation did not reach statistical significance when dichotomized at the moderate severity threshold (Table 3).

Addition of these echocardiographic parameters to the STS-PROMM resulted in a net improvement in model performance as evidenced by an increase in c-statistic from 0.68 to 0.73, a decrease in AIC from 543 to 470, an NRI of 27.5% (95% CI 12.8%, 42.1%) and IDI of 5.9% (95% CI 2.8% to 8.9%) (Figure 2). The incremental value was greatest in patients at intermediate risk as the maximal increase in c-statistic was observed in those with STS-PROMM 10-25%. After adjusting for STS-PROMM, restrictive LV diastolic filling (OR 2.38; 95% CI 1.21, 4.70) and RV fractional area change (OR 0.73; 95% CI 0.55, 0.98) remained independently predictive.

Seventy-three (10.9%) deaths were observed over a median follow-up of 3.2 years (Q1 2.5, Q3 3.9 years). In the Cox proportional hazards model, two echocardiographic parameters were found to be predictive of all-cause mortality: RV fractional area change (HR 0.73; 95% CI 0.57, 0.95) and PASP (HR 1.03; 95% CI 1.01 to 1.05) (Table 3). In particular, patients with a preoperative PASP ≥50 mmHg had a threefold increase in mortality (HR 3.54; 95% CI 1.95, 6.42) (Figure 3).

In sensitivity analyses, the same echocardiographic predictors were identified when individual clinical covariables were used instead of the composite STS-PROMM to adjust for
baseline characteristics (Supplementary Tables 2 and 3), and when multiple imputation was used to derive values for missing PASP (N=175 missing due to insufficient tricuspid regurgitation jet envelope).

Validation Cohort

A total of 236 patients underwent isolated CABG at the validation site, of which 187 had available preoperative echocardiograms performed within 30 days at the study center. Compared to the derivation cohort, the validation cohort demonstrated slightly lower mean age (65.8 ± 10.3 vs. 67.2 ± 11.1), lower proportion of females (17.6% vs. 22.8%), and lower mean STS-PROMM (13.8 ± 12.1% vs. 19.1 ± 13.3%) (Supplementary Table 4). Thirty-three (17.6%) postoperative mortalities or major morbidities were observed during the index hospitalization. When the echocardiographic parameters tested in the derivation cohort were re-entered, the AIC model selection procedure identified restrictive LV diastolic filling (OR 4.73; 95% CI 1.11, 20.06), abnormal RV myocardial performance index (OR 2.54; 95% CI 1.04, 6.22), and mitral regurgitation (OR 1.65; 95% CI 0.99, 2.76) as the optimal predictors of mortality or major morbidity. Abnormal RV fractional area change was a strong predictor in univariate analysis (OR 8.93; 95% 2.02, 39.50) but it was not statistically significant in multivariable analysis, partly due to its lower prevalence in the validation cohort (6.1% vs. 10.0%). The model coefficients fit in the derivation set were applied to the validation set and used to calculate the c-statistic for the STS-PROMM alone vs. the STS-PROMM plus the echocardiographic parameters. Addition of the echocardiographic parameters resulted in a similar net improvement in model performance as evidenced by an increase in c-statistic from 0.73 to 0.76.

Discussion

Our study has demonstrated the prognostic impact of a comprehensive echocardiogram in
patients undergoing CABG. Preoperative RV dysfunction and restrictive LV filling emerged as powerful predictors of mortality or major morbidity after CABG, whereas RV dysfunction and pulmonary hypertension predicted long-term mortality over 3.2 years. Importantly, addition of these echocardiographic parameters to the STS risk score resulted in a net improvement in model performance, signifying that echocardiography yielded incremental value.

The incremental value provided by the echocardiogram above traditional risk scores was found to be substantive. The increase in c-statistic of 0.03-0.05 and IDI of 5.9% compare favorably with other commonly used prognostic tests such as coronary artery calcium testing (increase in c-statistic +0.04, IDI 1.5%) or high-sensitivity c-reactive protein testing (increase in c-statistic +0.01, IDI 0.2%) above traditional risk factors to predict incident cardiovascular events. The modest baseline c-statistic of 0.68 to predict major morbidity in this study is consistent with prior reports (c-statistic 0.65-0.70 to predict morbidity vs. 0.75-0.80 to predict mortality) and confirms the limitations in predicting who will suffer a postoperative complication.

Inclusion of RV dysfunction and restrictive LV filling in risk scores would lead to refined estimates of operative risk, which have historically been less accurate in certain patients, particularly the elderly. Using echocardiography to improve risk prediction would allow clinicians and patients to be better informed in their shared decision-making and planning. Since higher-risk patients are often those that derive greater benefits from revascularization, the main clinical utility of echocardiography in identifying higher-risk patients would not be to withhold CABG from such patients but rather to tailor the revascularization strategy to the individual patient. For example, a patient found to have preoperative RV dysfunction and/or restrictive LV filling may potentially benefit from a less invasive revascularization strategy (minimally invasive
CABG, off-pump CABG, multivessel PCI. Carefully designed prospective studies are needed to test and validate this hypothesis.

Intraoperative transesophageal echocardiography (TEE), now commonly performed in many centers, provides valuable guidance for intraoperative management during CABG. However, the mandate and focus of the intraoperative TEE is clearly different than that of the preoperative transthoracic exam. The preoperative transthoracic exam offers a comprehensive assessment of the severity and extent of disease, and in doing so, exerts a direct influence on patient selection and revascularization strategy. The intraoperative TEE is performed at a time when the revascularization strategy has in large part already been determined and would be impractical to change. Thus, the preoperative transthoracic exam and the intraoperative TEE serve complimentary (as opposed to redundant) roles.

Beyond guiding the overall revascularization strategy, specific interventions aimed at a given echocardiographic abnormality could be employed. For the severely dysfunctional RV (abnormal RV FAC), right ventricular assist devices have been successfully used as adjuncts to CABG\textsuperscript{18,19}. For the mildly dysfunctional RV, ischemic preconditioning by transient aortic cross-clamping and reperfusion showed positive results although these have yet to be applied in clinical practice\textsuperscript{20}. Revascularization of intermediate right coronary artery stenoses does not seem to be a predictor of RV recovery after CABG\textsuperscript{21,22}. For patients with pulmonary hypertension, pulmonary vasodilators have been shown to improve outcomes\textsuperscript{23,24}. For the restrictive LV, milrinone has had mixed results\textsuperscript{25,26} whereas close monitoring and optimization of volume status and filling pressures remains the mainstay.

Preoperative RV dysfunction was a strong predictor of short- and long-term outcomes after CABG. Previously, the clinical impact of preoperative RV dysfunction was unclear. One
series of 74 patients showed that tricuspid annular plane systolic excursion was not predictive of death or readmission after CABG27, whereas another series of 41 patients with severe LV dysfunction showed that RV FAC assessed by intraoperative TEE was predictive of ventilator hours and inotrope requirements in the early postoperative period28. The latter study was difficult to extrapolate since RV FAC had been measured under anesthetized conditions, in a highly selected patient population, with a small sample size underpowered to detect differences in clinical endpoints (only 7 patients had an abnormal RV FAC). Our series of 667 diverse patients has shown more definitively that RV FAC assessed by resting preoperative TTE was predictive of major clinical endpoints.

In addition to RV FAC as a measure of RV systolic dysfunction, our echocardiographic protocol included RV MPI as a measure of global RV efficiency. These two measures proved to be complementary – RV FAC identified a small group of patients (5%) with overt RV hypokinesis that were at extreme risk (50% observed mortality or major morbidity), whereas RV MPI identified a larger group (24%) with subclinical RV impairment which may not otherwise be detected by visual assessment of the RV that were at high risk (26% observed mortality or major morbidity). We opted not to include measures of longitudinal RV function (tricuspid annular plane systolic excursion or tricuspid annular tissue Doppler velocity) for two reasons: first, these have been shown to inaccurately correlate with postoperative RV ejection fraction29 or functional capacity30 after cardiac surgery, and second, these require dedicated M-Mode and tissue Doppler acquisitions which are not always available. RV FAC and MPI have the distinct advantage of being measurable offline from routinely acquired images within <5 minutes. These two parameters are recommended for routine clinical use by the Guidelines for the Echocardiographic Assessment of the Right Heart from the American Society of
Echocardiography as their reliability and prognostic value have been extensively validated.

Restrictive LV filling, the echocardiographic hallmark of severe diastolic dysfunction, was the other independent predictor of mortality or major morbidity in our cohort. This finding is consistent with prior studies which have consistently shown that severe but not mild or moderate diastolic dysfunction is associated with mortality and complications after CABG. The prevalence of restrictive LV filling was 6-10% in our two cohorts, in line with prior studies. This prevalence may vary depending on the patient population studied (3% in elective low-risk patients up to 48% in high-risk patients with severe LV systolic dysfunction).

The rationale for RV dysfunction and restrictive LV diastolic filling as determinants of postoperative mortality or major morbidity can be appreciated by reviewing the usual physiological changes after CABG. Two of the predominant disturbances are (a) altered RV contraction and relaxation observed at the time of pericardial opening, and (b) increased LV stiffness due to myocardial edema and extrinsic compressive forces. Thus, given the expected decline in RV performance and LV stiffness after CABG, patients with preoperative findings of abnormal RV performance and/or LV stiffness (severe diastolic dysfunction) are at a clear disadvantage. Conversely, CABG is associated with improved LV relaxation due in part to relief of ischemia, which may explain why patients with preoperative findings of abnormal LV relaxation (mild-to-moderate diastolic dysfunction) do not face an increase in adverse events. Additionally, severe diastolic dysfunction as measured by a mitral inflow deceleration time <150 ms has been shown to be a surrogate marker for viability (or lack thereof) validated against dobutamine echocardiography and myocardial scintigraphy; this may explain, in part, why patients with restrictive LV filling tend to deteriorate rather than improve after CABG.

By analyzing the comprehensive echocardiogram rather than individual parameters of
interest, our study was able to adjust for confounding between echocardiographic parameters. Prior studies have been limited by partial adjustment for confounding, often adjusting for basic clinical variables but no other echocardiographic variables, leading to inconsistent results. For example, the effect of low LVEF on postoperative mortality has been reported to be highly significant when adjusted for basic clinical variables\textsuperscript{40-42} but nonsignificant when adjusted for left ventricular size and diastolic function\textsuperscript{31,43}. Our data reflect this, with the effect of low LVEF being highly significant in univariate analysis (OR 5.2, P<0.001) but nonsignificant when diastolic dysfunction and RV dysfunction were entered in the multivariable model (OR 1.8, P=NS). Irrespective of these potential confounders, it is not surprising that LVEF was nonsignificant in our contemporary cohorts since the prognostic impact of LVEF has been steadily declining in parallel with improvements in surgical techniques and post-operative care\textsuperscript{44,45}.

A number of limitations should be acknowledged. First, the STS composite endpoint used as our primary outcome is intended to capture representative major morbidities after cardiac surgery, including deep sternal wound infection which is of questionable relevance to preoperative echocardiography. However, deep sternal wound infection contributed very few events (N=4) to the composite endpoint and a sensitivity analysis excluding it was unchanged. Second, follow-up echocardiography is not routinely performed after CABG, precluding the assessment of functional recovery as an outcome measure. Third, approximately one third of patients undergoing CABG in the derivation cohort and one fifth in the validation cohort did not have a recent preoperative echocardiogram; these tended to be lower risk patients. Although this non-random subset could have affected the generalizability of our findings, the derivation and validation cohorts still included a large number of low risk patients who were ultimately found to
derive a similar if not greater incremental value from the echocardiogram. Fourth, although a formal cost-effectiveness analysis was not performed, it is encouraging to note that the cost savings of preventing one postoperative major morbidity (average additive cost $40,704-$62,773\(^{46}\)) would offset the cost of performing >200 preoperative echocardiograms (global cost $233 as per the 2011 ASE Coding and Reimbursement Newsletter). Fifth, since the STS-PROMM was not designed nor validated to predict long-term mortality, the incremental value of echocardiographic predictors over such a clinical risk score was not assessed for this outcome measure. Lastly, the effect of significant MR was equivocal (it was identified by the model selection procedure as one of four important predictors, yet it did not reach statistical significance) and the study was not designed to address how significant MR should be managed at the time of CABG. This remains a controversial question which will be most appropriately answered by ongoing randomized clinical trials.

The strengths of this study include a multi-center design with derivation and validation cohorts, and a comprehensive echocardiographic protocol including right heart parameters which had previously been less thoroughly evaluated. Our findings serve as an impetus to begin to integrate measures of RV dysfunction and severe LV diastolic dysfunction in the preoperative assessment of risk before CABG.

**Acknowledgements:** We would like to thank Marcia Leavitt, David Crowell, and Karen Lynch for their invaluable help in obtaining clinical and echocardiographic data for this study. We would also like to thank all of the cardiac sonographers at the Massachusetts General Hospital and Jewish General Hospital for their excellence in acquiring the echocardiographic images that made this study possible.

**Funding Sources:** Dr. Jonathan Afilalo was supported by the FRSQ (Fonds de Recherché Santé
du Québec) Research Fellowship Award. This work was conducted with support from Harvard Catalyst | The Harvard Clinical and Translational Science Center (NIH Award #UL1 RR 025758 and financial contributions from Harvard University and its affiliated academic health care centers). The content is solely the responsibility of the authors and does not necessarily represent the official views of Harvard Catalyst, Harvard University and its affiliated academic health care centers, the National Center for Research Resources, or the National Institutes of Health.

**Conflict of Interest Disclosures:** The authors have no conflicts of interest to disclose. Jonathan Afilalo had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**References:**


39. Hedman A, Samad BA, Larsson T, Zuber E, Nordlander R, Alam M. Improvement in


# Table 1. Clinical Characteristics

<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>Overall (N=667)</th>
<th>Mortality or Major Morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>67.2 ± 11.1</td>
<td>70.5 ± 11.2</td>
</tr>
<tr>
<td>Female</td>
<td>152 (22.8)</td>
<td>26 (25.0)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.8 ± 5.2</td>
<td>28.3 ± 4.5</td>
</tr>
<tr>
<td>Diabetes</td>
<td>250 (37.5)</td>
<td>42 (40.4)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>247 (37.0)</td>
<td>55 (52.9)</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>85 (12.7)</td>
<td>16 (15.4)</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>138 (20.7)</td>
<td>30 (28.8)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>119 (17.8)</td>
<td>23 (22.1)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>70 (10.5)</td>
<td>21 (20.2)</td>
</tr>
<tr>
<td>Prior cardiac surgery</td>
<td>27 (4.0)</td>
<td>7 (6.7)</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>3 (0.4)</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>CHF within 2 weeks</td>
<td>195 (29.2)</td>
<td>56 (53.8)</td>
</tr>
<tr>
<td>STS predicted mortality/morbidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>19.1 ± 13.3</td>
<td>17.7 ± 12.2</td>
</tr>
<tr>
<td>Low risk (0-10%)</td>
<td>194 (29.1)</td>
<td>13 (12.9)</td>
</tr>
<tr>
<td>Intermediate risk (10-25%)</td>
<td>309 (46.3)</td>
<td>48 (36.6)</td>
</tr>
<tr>
<td>High risk (&gt;25%)</td>
<td>164 (24.6)</td>
<td>53 (50.5)</td>
</tr>
<tr>
<td>Cardiac presentation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No symptoms</td>
<td>37 (7.8)</td>
<td>7 (10.1)</td>
</tr>
<tr>
<td>Stable angina</td>
<td>81 (17.2)</td>
<td>12 (17.4)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>156 (33.1)</td>
<td>13 (18.8)</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>151 (32.0)</td>
<td>24 (34.8)</td>
</tr>
<tr>
<td>STEMI</td>
<td>47 (10.0)</td>
<td>13 (18.8)</td>
</tr>
<tr>
<td>Operative status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elective</td>
<td>67 (10.0)</td>
<td>7 (6.7)</td>
</tr>
<tr>
<td>Urgent</td>
<td>598 (89.7)</td>
<td>96 (92.3)</td>
</tr>
<tr>
<td>Emergent</td>
<td>2 (0.3)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Number of grafts</td>
<td>3.3 ± 1.1</td>
<td>3.3 ± 1.2</td>
</tr>
<tr>
<td>In-hospital outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality or major morbidity</td>
<td>104 (15.6)</td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>11 (1.6)</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>11 (1.6)</td>
<td></td>
</tr>
<tr>
<td>Renal failure</td>
<td>23 (3.4)</td>
<td></td>
</tr>
<tr>
<td>Prolonged intubation</td>
<td>68 (10.2)</td>
<td></td>
</tr>
<tr>
<td>Deep sternal wound infection</td>
<td>4 (0.6)</td>
<td></td>
</tr>
<tr>
<td>Reoperation</td>
<td>44 (6.6)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; CHF, congestive heart failure; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; STS-PROMM, Society of Thoracic Surgeons predicted risk of mortality or major morbidity.
Table 2. Preoperative Echocardiographic Parameters

<table>
<thead>
<tr>
<th></th>
<th>Overall (N=667)</th>
<th>Mortality or Major Morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA end-diastolic area index, cm^2</td>
<td>8.2 ± 2.2</td>
<td>60.1 ± 21.8</td>
</tr>
<tr>
<td>LA volume index, mL/m^2</td>
<td>31.4 ± 12.2</td>
<td>35.3 ± 12.5</td>
</tr>
<tr>
<td>LA linear dimension (PLAX), cm</td>
<td>3.8 ± 0.6</td>
<td>3.8 ± 0.6</td>
</tr>
<tr>
<td>LV end-diastolic volume index, mL/m^2</td>
<td>53.1 ± 18.3</td>
<td>60.1 ± 21.8</td>
</tr>
<tr>
<td>RV myocardial performance index</td>
<td>0.33 ± 0.15</td>
<td>0.40 ± 0.18</td>
</tr>
<tr>
<td>LV end-diastolic linear dimension, cm</td>
<td>4.7 ± 0.7</td>
<td>4.7 ± 0.8</td>
</tr>
<tr>
<td>PASP, mmHg</td>
<td>38.2 ± 11.8</td>
<td>42.4 ± 15.4</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>55.3 ± 12.7</td>
<td>49.9 ± 14.8</td>
</tr>
<tr>
<td>RV area index, cm^2</td>
<td>7.3 ± 2.1</td>
<td>7.9 ± 2.0</td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>237 (35.5)</td>
<td>26 (25.0)</td>
</tr>
<tr>
<td>Mild</td>
<td>225 (33.7)</td>
<td>28 (26.9)</td>
</tr>
<tr>
<td>Moderate</td>
<td>103 (15.4)</td>
<td>18 (17.3)</td>
</tr>
<tr>
<td>Pseudonormal</td>
<td>103 (15.4)</td>
<td>18 (17.3)</td>
</tr>
<tr>
<td>Restrictive</td>
<td>67 (10.0)</td>
<td>25 (24.0)</td>
</tr>
<tr>
<td>N/A</td>
<td>35 (5.3)</td>
<td>7 (6.7)</td>
</tr>
<tr>
<td>LV mass index, g/m^2</td>
<td>94.6 ± 24.0</td>
<td>99.8 ± 25.6</td>
</tr>
<tr>
<td>Tricuspid regurgitation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None-Trivial</td>
<td>392 (58.8)</td>
<td>45 (43.3)</td>
</tr>
<tr>
<td>Mild</td>
<td>222 (33.3)</td>
<td>41 (39.4)</td>
</tr>
<tr>
<td>Moderate</td>
<td>53 (7.9)</td>
<td>18 (17.3)</td>
</tr>
<tr>
<td>RA area index, cm^2</td>
<td>7.3 ± 2.1</td>
<td>7.9 ± 2.0</td>
</tr>
<tr>
<td>RV end-diastolic linear dimension, cm</td>
<td>8.2 ± 2.2</td>
<td>8.7 ± 2.4</td>
</tr>
<tr>
<td>RV fractional area change, %</td>
<td>50.2 ± 9.3</td>
<td>45.8 ± 11.6</td>
</tr>
<tr>
<td>PASP, mmHg</td>
<td>38.2 ± 11.8</td>
<td>42.4 ± 15.4</td>
</tr>
<tr>
<td>RA area index, cm^2</td>
<td>7.3 ± 2.1</td>
<td>7.9 ± 2.0</td>
</tr>
<tr>
<td>Pseudonormal</td>
<td>103 (15.4)</td>
<td>18 (17.3)</td>
</tr>
<tr>
<td>Restrictive</td>
<td>67 (10.0)</td>
<td>25 (24.0)</td>
</tr>
<tr>
<td>N/A</td>
<td>35 (5.3)</td>
<td>7 (6.7)</td>
</tr>
<tr>
<td>PASP, mmHg</td>
<td>38.2 ± 11.8</td>
<td>42.4 ± 15.4</td>
</tr>
<tr>
<td>Tricuspid regurgitation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None-Trivial</td>
<td>482 (72.3)</td>
<td>65 (62.5)</td>
</tr>
<tr>
<td>Mild</td>
<td>156 (23.4)</td>
<td>28 (26.9)</td>
</tr>
<tr>
<td>Moderate</td>
<td>29 (4.3)</td>
<td>11 (10.6)</td>
</tr>
</tbody>
</table>

Abbreviations: LA, left atrial; LV, left ventricular; PLAX, parasternal long-axis view; LVEF, left ventricular ejection fraction; N/A, not available; RA, right atrial; RV, right ventricular; PASP, pulmonary artery systolic pressure.
**Table 3. Optimal Echocardiographic Predictors in Multivariable Analysis**

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Continuous</td>
<td>Dichotomous</td>
</tr>
<tr>
<td>In-hospital mortality or major morbidity (104 events)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe LV diastolic dysfunction (restrictive filling pattern)</td>
<td>2.39 (1.26, 4.55; P=0.008)</td>
<td>2.96 (1.59, 5.49; P=0.001)</td>
</tr>
<tr>
<td>RV systolic dysfunction (fractional area change)</td>
<td>0.73 (0.56, 0.95; P=0.02)</td>
<td>3.03 (1.28, 7.20; P=0.01)</td>
</tr>
<tr>
<td>RV inefficiency (myocardial performance index)</td>
<td>1.44 (1.10, 1.90; P=0.009)</td>
<td>1.89 (1.13, 3.15; P=0.02)</td>
</tr>
<tr>
<td>Mitral regurgitation (grade 0-4)</td>
<td>1.44 (1.04, 2.01; P=0.03)</td>
<td>1.96 (0.96, 4.02; P=0.07)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>HR (95% CI)</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Continuous</td>
<td>Dichotomous</td>
</tr>
<tr>
<td>All-cause mortality at 3.2 years (73 events)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV systolic dysfunction (fractional area change)</td>
<td>0.73 (0.57, 0.95; P=0.01)</td>
<td>2.03 (0.95, 4.33; P=0.07)</td>
</tr>
<tr>
<td>Pulmonary artery systolic pressure (mmHg)</td>
<td>1.03 (1.01, 1.05; P=0.001)</td>
<td>3.54 (1.95, 6.42; P&lt;0.001)</td>
</tr>
</tbody>
</table>

*Continuous predictors* denotes entry of continuous echocardiographic variables in their continuous form (RV fractional area change and RV myocardial performance index were standardized such that the OR and HR are per SD change).

**Dichotomous predictors** denotes entry of continuous echocardiographic variables in a transformed dichotomous form according to ASE guidelines and normal reference limits (RV fractional area change <35%, RV myocardial performance index >0.4, Mitral regurgitation severity ≥moderate, Pulmonary artery systolic pressure ≥50 mmHg).

Abbreviations: LV, left ventricular; RV, right ventricular; OR, odds ratio; HR, hazard ratio; CI, confidence interval.
Figure Legends:

Figure 1. Flow Diagram for the Main Derivation Cohort. Out of 1,150 patients that had isolated CABG at the Massachusetts General Hospital in the study period, 667 met the inclusion criteria and were considered in the analyses.

Figure 2. Incremental Value of Echocardiography When Added to the STS Risk Score. ROC curve for the STS risk score alone and the STS risk score plus the echocardiographic parameters to predict mortality or major morbidity.

1,150 patients underwent isolated CABG between 2007-2009

434 patients did not have preoperative echocardiography

49 had preoperative echocardiography at another center

667 patients were included
Figure 3b

Kaplan-Meier survival estimates

Survival

Follow-up time after CABG (days)

PASP n/a

PASP <50 mmHg

PASP ≥50 mmHg
Incremental Value of the Preoperative Echocardiogram to Predict Mortality and Major Morbidity in Coronary Artery Bypass Surgery

Circulation. published online December 12, 2012;
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/early/2012/12/12/CIRCULATIONAHA.112.127639

Data Supplement (unedited) at:
http://circ.ahajournals.org/content/suppl/2012/12/12/CIRCULATIONAHA.112.127639.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/
Incremental Value of the Preoperative Echocardiogram to Predict Mortality and Major Morbidity in Coronary Artery Bypass Surgery

SUPPLEMENTAL MATERIAL
Supplementary Table 1: Characteristics of Included vs. Excluded Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Included (N=667)</th>
<th>Excluded (N=483)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>67.2 ± 11.1</td>
<td>67.8 ± 9.7</td>
</tr>
<tr>
<td>Female</td>
<td>152 (22.8)</td>
<td>67 (13.9)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.8 ± 5.2</td>
<td>29.0 ± 5.1</td>
</tr>
<tr>
<td>Diabetes</td>
<td>250 (37.5)</td>
<td>159 (32.9)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>247 (37.0)</td>
<td>109 (22.7)</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>85 (12.7)</td>
<td>44 (9.1)</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>138 (20.7)</td>
<td>68 (14.1)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>119 (17.8)</td>
<td>69 (14.3)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>70 (10.5)</td>
<td>30 (6.2)</td>
</tr>
<tr>
<td>Prior cardiac surgery</td>
<td>27 (4.0)</td>
<td>29 (6.0)</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>3 (0.4)</td>
<td>4 (0.8)</td>
</tr>
<tr>
<td>CHF within 2 weeks</td>
<td>195 (29.2)</td>
<td>32 (6.6) *</td>
</tr>
<tr>
<td>Cardiac presentation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No symptoms</td>
<td>37 (7.8)</td>
<td>48 (15.5)</td>
</tr>
<tr>
<td>Stable angina</td>
<td>81 (17.2)</td>
<td>129 (41.8)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>156 (33.1)</td>
<td>99 (32.0)</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>151 (32.0)</td>
<td>25 (8.1) *</td>
</tr>
<tr>
<td>STEMI</td>
<td>47 (10.0)</td>
<td>8 (2.6) *</td>
</tr>
<tr>
<td>Operative status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elective</td>
<td>67 (10.0)</td>
<td>267 (55.3)</td>
</tr>
<tr>
<td>Urgent</td>
<td>598 (89.7)</td>
<td>208 (43.1) *</td>
</tr>
<tr>
<td>Emergent</td>
<td>2 (0.3)</td>
<td>8 (1.7)</td>
</tr>
<tr>
<td>LVEF (clinically reported value)</td>
<td>57.4 ± 14.5</td>
<td>60.0 ± 13.5</td>
</tr>
<tr>
<td>STS-PROMM</td>
<td>19.1 ± 13.3</td>
<td>12.2 ± 9.2</td>
</tr>
<tr>
<td>In-hospital outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality or major morbidity</td>
<td>104 (15.6)</td>
<td>47 (9.7)</td>
</tr>
<tr>
<td>Mortality</td>
<td>11 (1.6)</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Stroke</td>
<td>11 (1.6)</td>
<td>3 (0.6)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>23 (3.4)</td>
<td>9 (1.9)</td>
</tr>
<tr>
<td>Prolonged intubation</td>
<td>68 (10.2)</td>
<td>21 (4.3)</td>
</tr>
<tr>
<td>Deep sternal wound infection</td>
<td>4 (0.6)</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Reoperation</td>
<td>44 (6.6)</td>
<td>21 (4.3)</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; CHF, congestive heart failure; STEMI, ST-elevation myocardial infarction; NSTEMI, non-STEMI; LVEF, left ventricular ejection fraction; STS-PROMM, Society of Thoracic Surgeons predicted risk of mortality or major morbidity.
* CHF, NSTEMI/STEMI presentation, and urgent operative status were associated with having a preoperative echocardiogram in multivariable analysis.

‡ 132 patients in the excluded group did not have any assessment of valvular function (compared to 0 patients in the included group).
Supplementary Table 2: Logistic Model with Echocardiographic and Clinical Covariables to Predict In-Hospital Mortality or Major Morbidity

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, per year</td>
<td>1.00 (0.97, 1.03)</td>
</tr>
<tr>
<td>Female</td>
<td>1.42 (0.76, 2.67)</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>0.94 (0.45, 1.95)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>1.34 (0.72, 2.49)</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>1.14 (0.62, 2.08)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>1.23 (0.66, 2.30)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.87 (0.51, 1.48)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>2.18 (1.10, 4.33)</td>
</tr>
<tr>
<td>Redo surgery</td>
<td>2.01 (0.70, 5.82)</td>
</tr>
<tr>
<td>LV end-diastolic volume index, per mL/m²</td>
<td>1.02 (1.00, 1.03)</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td></td>
</tr>
<tr>
<td>&lt;30%</td>
<td>1.40 (0.50, 3.89)</td>
</tr>
<tr>
<td>30-49%</td>
<td>1.15 (0.59, 2.23)</td>
</tr>
<tr>
<td>50-69%</td>
<td>Referent</td>
</tr>
<tr>
<td>&gt;=70%</td>
<td>2.17 (0.95, 4.92)</td>
</tr>
<tr>
<td>LV restrictive diastolic filling</td>
<td>2.33 (1.15, 4.71)</td>
</tr>
<tr>
<td>LV mass index, per g/m²</td>
<td>0.99 (0.98, 1.01)</td>
</tr>
<tr>
<td>Mitral regurgitation, per grade</td>
<td>1.20 (0.82, 1.75)</td>
</tr>
<tr>
<td>RV area index, per cm²/m²</td>
<td>1.04 (0.92, 1.17)</td>
</tr>
<tr>
<td>RV fractional area change, per %</td>
<td>0.74 (0.55, 0.99)</td>
</tr>
<tr>
<td>RV myocardial performance index, per unit</td>
<td>1.37 (1.01, 1.87)</td>
</tr>
<tr>
<td>Pulmonary artery systolic pressure &gt;=50 mmHg</td>
<td>0.85 (0.39, 1.88)</td>
</tr>
<tr>
<td>Tricuspid regurgitation, per grade</td>
<td>0.98 (0.63, 1.51)</td>
</tr>
</tbody>
</table>

The AIC model selection procedure identified the following optimal model:

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV restrictive diastolic filling</td>
<td>1.59 (0.97, 2.61)</td>
</tr>
<tr>
<td>RV fractional area change, per %</td>
<td>1.01 (1.00, 1.03)</td>
</tr>
<tr>
<td>RV myocardial performance index, per unit</td>
<td>1.55 (0.85, 2.82)</td>
</tr>
<tr>
<td>LV end-diastolic volume index, per mL/m²</td>
<td>2.18 (1.15, 4.14)</td>
</tr>
<tr>
<td>Female</td>
<td>2.38 (1.24, 4.57)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>1.36 (1.02, 1.80)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>0.71 (0.54, 0.94)</td>
</tr>
</tbody>
</table>
Supplementary Table 3: Cox Proportional Hazards Model with Echocardiographic and Clinical Covariables to Predict Long-Term Mortality

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, per year</td>
<td>0.99 (0.96, 1.02)</td>
</tr>
<tr>
<td>Female</td>
<td>0.91 (0.46, 1.77)</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>1.58 (0.85, 2.96)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>2.22 (1.14, 4.33)</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>1.69 (0.96, 3.01)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>2.39 (1.32, 4.33)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2.44 (1.38, 4.31)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1.36 (0.64, 2.88)</td>
</tr>
<tr>
<td>Redo surgery</td>
<td>0.99 (0.29, 3.37)</td>
</tr>
<tr>
<td>LV end-diastolic volume index, per mL/m²</td>
<td>1.00 (0.98, 1.02)</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td></td>
</tr>
<tr>
<td>&lt;30%</td>
<td>0.55 (0.16, 1.82)</td>
</tr>
<tr>
<td>30-49%</td>
<td>1.66 (0.87, 3.20)</td>
</tr>
<tr>
<td>50-69%</td>
<td>Referent</td>
</tr>
<tr>
<td>&gt;=70%</td>
<td>1.45 (0.58, 3.65)</td>
</tr>
<tr>
<td>LV restrictive diastolic filling</td>
<td>0.60 (0.27, 1.35)</td>
</tr>
<tr>
<td>LV mass index, per g/m²</td>
<td>1.00 (0.99, 1.01)</td>
</tr>
<tr>
<td>Mitral regurgitation, per grade</td>
<td>1.09 (0.73, 1.63)</td>
</tr>
<tr>
<td>RV area index, per cm²/m²</td>
<td>0.99 (0.87, 1.12)</td>
</tr>
<tr>
<td>RV fractional area change, per %</td>
<td>0.71 (0.52, 0.97)</td>
</tr>
<tr>
<td>RV myocardial performance index, per unit</td>
<td>1.22 (0.89, 1.68)</td>
</tr>
<tr>
<td>Pulmonary artery systolic pressure &gt;=50 mmHg</td>
<td>1.62 (0.79, 3.32)</td>
</tr>
<tr>
<td>Tricuspid regurgitation, per grade</td>
<td>1.08 (0.70, 1.65)</td>
</tr>
</tbody>
</table>

The AIC model selection procedure identified the following optimal model:

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary artery systolic pressure &gt;=50 mmHg</td>
<td>1.93 (1.05, 3.57)</td>
</tr>
<tr>
<td>RV fractional area change, per %</td>
<td>0.77 (0.61, 0.99)</td>
</tr>
<tr>
<td>LV ejection fraction 30-49%</td>
<td>1.82 (1.05, 3.14)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>2.34 (1.32, 4.15)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.22 (1.29, 3.84)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>2.39 (1.37, 4.18)</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>1.72 (1.01, 2.92)</td>
</tr>
</tbody>
</table>
**Supplementary Table 4: Clinical and Echocardiographic Characteristics of Patients in the Validation Cohort**

<table>
<thead>
<tr>
<th>Clinical</th>
<th>N=187</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CLINICAL</strong></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>65.8 ± 10.3</td>
</tr>
<tr>
<td>Female</td>
<td>33 (17.6)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.7 ± 4.4</td>
</tr>
<tr>
<td>Diabetes</td>
<td>76 (40.6)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>48 (25.7)</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>14 (7.5)</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>26 (13.9)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>21 (11.2)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>16 (8.6)</td>
</tr>
<tr>
<td>Prior cardiac surgery</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>4 (2.1)</td>
</tr>
<tr>
<td>CHF within 2 weeks</td>
<td>37 (21.3)</td>
</tr>
<tr>
<td>Cardiac presentation</td>
<td></td>
</tr>
<tr>
<td>No symptoms</td>
<td>3 (1.6)</td>
</tr>
<tr>
<td>Stable angina</td>
<td>39 (20.9)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>66 (35.3)</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>67 (35.8)</td>
</tr>
<tr>
<td>STEMI</td>
<td>12 (6.4)</td>
</tr>
<tr>
<td>Operative status</td>
<td></td>
</tr>
<tr>
<td>Elective</td>
<td>53 (28.3)</td>
</tr>
<tr>
<td>Urgent</td>
<td>128 (68.4)</td>
</tr>
<tr>
<td>Emergent</td>
<td>6 (3.2)</td>
</tr>
<tr>
<td>STS-PROMM</td>
<td>13.8 ± 12.1</td>
</tr>
<tr>
<td>In-hospital outcomes</td>
<td></td>
</tr>
<tr>
<td>Mortality or major morbidity</td>
<td>33 (17.6)</td>
</tr>
<tr>
<td>Mortality</td>
<td>3 (1.6)</td>
</tr>
<tr>
<td>Stroke</td>
<td>2 (1.1)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>5 (2.7)</td>
</tr>
<tr>
<td>Prolonged intubation</td>
<td>19 (10.2)</td>
</tr>
<tr>
<td>Deep sternal wound infection</td>
<td>2 (1.1)</td>
</tr>
<tr>
<td>Reoperation</td>
<td>15 (8.0)</td>
</tr>
<tr>
<td><strong>ECHOCARDIOGRAPHIC</strong></td>
<td></td>
</tr>
<tr>
<td>LA volume index, mL/m²</td>
<td>24.1 ± 10.1</td>
</tr>
<tr>
<td>LV end-diastolic volume index, mL/m²</td>
<td>41.6 ± 18.9</td>
</tr>
<tr>
<td>LV end-diastolic linear dimension, cm</td>
<td>4.8 ± 0.6</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>54.8 ± 14.3</td>
</tr>
<tr>
<td>LVEF</td>
<td>13 (7.1)</td>
</tr>
<tr>
<td>---------------------</td>
<td>----------</td>
</tr>
<tr>
<td>&lt;30%</td>
<td></td>
</tr>
<tr>
<td>30-49%</td>
<td></td>
</tr>
<tr>
<td>50-69%</td>
<td></td>
</tr>
<tr>
<td>≥70%</td>
<td></td>
</tr>
</tbody>
</table>

| Diastolic filling   |          |           |            |           |
| Normal              | 72 (39.8) |          |            |           |
| Impaired            | 54 (29.8) |          |            |           |
| Pseudonormal        | 27 (14.9) |          |            |           |
| Restrictive         | 11 (6.1)  |          |            |           |
| N/A                 | 17 (9.4)  |          |            |           |

| LV mass index, g/m2 | 84.2 ±23.6 |

| Mitral regurgitation|          |           |            |           |
| None-Trivial        | 119 (63.6) |          |            |           |
| Mild                | 59 (31.6)  |          |            |           |
| Moderate            | 9 (4.8)    |          |            |           |

| RA area index, cm/m2| 7.5 ±1.8  |
| RV end-diastolic area index, cm/m2 | 7.4 ±1.8 |
| RV fractional area change, %       | 49.3 ±9.0 |
| RV myocardial performance index    | 0.36 ±0.17 |
| PASP, mmHg                        | 34.2 ±10.5 |
| N/A                               | 62 (33.2)  |

| Tricuspid regurgitation|          |           |            |           |
| None-Trivial           | 137 (73.2) |          |            |           |
| Mild                   | 49 (26.2)  |          |            |           |
| Moderate               | 1 (0.5)    |          |            |           |

Abbreviations: BMI, body mass index; CHF, congestive heart failure; STEMI, ST-elevation myocardial infarction; NSTEMI, non-STEMI; LVEF, left ventricular ejection fraction; STS-PROMM, Society of Thoracic Surgeons predicted risk of mortality or major morbidity.